

WE CLAIM:

1. An ultrasound contrast agent comprising an aqueous suspension of gas filled microbubbles comprising a saturated phospholipid, a fatty acid, a hydrophilic stabilizer, and SF<sub>6</sub>, wherein the amount of the saturated phospholipid in the suspension is less than about 0.01% by weight.
2. The ultrasound contrast agent of claim 1, wherein the fatty acid is present in an amount between 1% and 50% by weight of the amount of the saturated phospholipid.
3. The ultrasound contrast agent of claim 1, wherein the fatty acid is present in an amount between 5% and 25% by weight of the amount of the saturated phospholipid.
4. The ultrasound contrast agent of claim 1, wherein the fatty acid is present in an amount between 10% and 15% by weight of the amount of the saturated phospholipid.
5. The ultrasound contrast agent of claim 1, wherein the fatty acid is a C<sub>12</sub>-C<sub>24</sub> straight chain saturated fatty acid selected from the group consisting of lauric acid, myristic acid, palmitic acid, stearic acid, arachidic acid, behenic acid, lignoceric acid and mixtures thereof.

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6. The ultrasound contrast agent of claim 1, wherein the fatty acid comprises palmitic acid in an amount between 10% and 15% by weight of the amount of the saturated phospholipid.
  7. The ultrasound contrast agent of claim 1, wherein the saturated phospholipid is selected from the group consisting of dimyristoylphosphatidic acid, dimyristoylphosphatidylglycerol, dimyristoylphosphatidylserine, dipalmitoylphosphatidic acid, dipalmitoylphosphatidylglycerol, dipalmitoylphosphatidylserine, distearoylphosphatidic acid, distearoylphosphatidylglycerol, distearoylphosphatidylserine and mixtures thereof.
  8. The ultrasound contrast agent of claim 1, wherein the saturated phospholipid comprises distearoylphosphatidylcholine (DSPC) and dipalmitoylphosphatidylglycerol (DPPG).
  9. The ultrasound contrast agent of any one of claims 1, 6 or 8 wherein the hydrophilic stabilizer comprises PEG 4000.
  10. The ultrasound contrast agent of claim 1, wherein the saturated phospholipid comprises distearoylphosphatidylcholine (DSPC) and dipalmitoylphosphatidylglycerol (DPPG), the fatty acid comprises palmitic acid in an amount between 10 and 15% by weight of the amount of the saturated phospholipid, and the hydrophilic stabilizer comprises PEG 4000.

11. A method of imaging a region of a body comprising :

- (a) administering to the body an aqueous suspension of gas filled microbubbles comprising a saturated phospholipid, a fatty acid, a hydrophilic stabilizer, and SF<sub>6</sub>, wherein the amount of the saturated phospholipid in the suspension is less than 0.01% by weight; and
- (b) imaging the body.

12. The method of imaging of claim 11, wherein the fatty acid is present in an amount between 1% and 50% by weight of the amount of the saturated phospholipid.

13. The method of imaging of claim 11, wherein the fatty acid is present in an amount between 5% and 25% by weight of the amount of the saturated phospholipid.

14. The method of imaging of claim 11, wherein the fatty acid is present in an amount between 10% and 15% by weight of the amount of the saturated phospholipid.

15. The method of imaging of claim 11, wherein the fatty acid is a C<sub>12</sub>-C<sub>24</sub> straight chain saturated fatty acid selected from the group consisting of lauric acid, myristic acid, palmitic acid, stearic acid, arachidic acid, behenic acid, lignoceric acid and mixtures thereof.

16. The method of imaging of claim 11, wherein the fatty acid comprises palmitic acid in an amount between 10% and 15% by weight of the amount of the saturated phospholipid.

17. The method of imaging of claim 11, wherein the saturated phospholipid is selected from the group consisting of dimyristoylphosphatidic acid, dimyristoylphosphatidylglycerol, dimyristoylphosphatidylserine, dipalmitoylphosphatidic acid, dipalmitoylphosphatidylglycerol, dipalmitoylphosphatidylserine, distearoylphosphatidic acid, distearoylphosphatidylglycerol, distearoylphosphatidylserine and mixtures thereof.
18. The method of imaging of claim 11, wherein the saturated phospholipid comprises distearoylphosphatidylcholine (DSPC) and dipalmitoylphosphatidylglycerol (DPPG).
19. The method of imaging of any one of claims 11, 16 or 18, wherein the hydrophilic stabilizer comprises PEG 4000.
20. The method of imaging of claim 11, wherein the saturated phospholipid comprises distearoylphosphatidylcholine (DSPC) and dipalmitoylphosphatidylglycerol (DPPG), the fatty acid comprises palmitic acid in an amount between 10% and 15% by weight of the amount of the saturated phospholipid, and the hydrophilic stabilizer comprises PEG 4000.
21. The method of imaging of claim 11, wherein the body is a vertebrate and the suspension is administered to the vasculature or body cavity of the vertebrate.

22. A dry formulation of an ultrasound contrast agent comprising a saturated phospholipid, a fatty acid, and a hydrophilic stabilizer, wherein upon dissolution in an aqueous carrier liquid, the dry formulation will form a suspension of microbubbles comprising SF<sub>6</sub> in which the amount of saturated phospholipid in the suspension is less than about 0.01% by weight.
23. The dry formulation of claim 22, wherein the fatty acid is present in an amount of between 1% and 50% by weight of the amount of the saturated phospholipid.
24. The dry formulation of claim 22, wherein the fatty acid is present in an amount of between 5% and 25% by weight of the amount of the saturated phospholipid.
25. The dry formulation of claim 22, wherein the fatty acid is present in an amount of between 10% and 15% by weight of the amount of the saturated phospholipid.
26. The dry formulation of claim 22, wherein the fatty acid is a C<sub>12</sub>-C<sub>24</sub> straight chain saturated fatty acid selected from the group consisting of lauric acid, myristic acid, palmitic acid, stearic acid, arachidic acid, behenic acid, lignoceric acid and mixtures thereof.
27. The dry formulation of claim 22, wherein the fatty acid comprises palmitic acid in an amount of between 10% and 15% by weight of the amount of the saturated phospholipid.

28. The dry formulation of claim 22, wherein the saturated phospholipid is selected from the group consisting of dimyristoylphosphatidic acid, dimyristoylphosphatidylglycerol, dimyristoylphosphatidylserine, dipalmitoylphosphatidic acid, dipalmitoylphosphatidylglycerol, dipalmitoylphosphatidylserine, distearoylphosphatidic acid, distearoylphosphatidylglycerol, distearoylphosphatidylserine and mixtures thereof.

29. The dry formulation of claim 22, wherein the saturated phospholipid comprises distearoylphosphatidylcholine (DSPC) and dipalmitoylphosphatidylglycerol (DPPG).

30. The dry formulation of any one of claims 22, 27 or 29, wherein the hydrophilic stabilizer comprises PEG 4000.

31. The dry formulation of claim 22, wherein the saturated phospholipid comprises distearoylphosphatidylcholine (DSPC) and dipalmitoylphosphatidylglycerol (DPPG), the fatty acid comprises palmitic acid in an amount of between 10% and 15% by weight of the amount of the saturated phospholipid, and the hydrophilic stabilizer comprises PEG 4000.

32. A method of using the dry formulation of any one of claims 22 to 29 or 31 for the preparation of an ultrasound contrast agent comprising forming a suspension of gas filled microbubbles with the dry formulation.

33. A method of preparing an ultrasound contrast agent comprising reconstituting the dry formulation of any one of claims 22 to 29 or 31 in an aqueous carrier liquid to form a suspension of gas filled microbubbles.

34. A method of imaging a region of a body comprising:

- (a) reconstituting the dry formulation of any one of claims 22 to 29 or 31 in an aqueous carrier liquid to form a suspension of gas filled microbubbles;
- (b) administering the suspension of gas filled microbubbles to the body; and
- (c) imaging the body.

35. A method of preparing a contrast agent comprising an aqueous suspension of gas filled microbubbles comprising SF<sub>6</sub> and saturated phospholipid, wherein the amount of saturated phospholipid in the suspension is less than about 0.01% by weight, the method comprising:

- (a) dissolving at least one saturated phospholipid, a fatty acid, and a hydrophilic stabilizer in an organic solvent to form a solution;
- (b) freeze drying or spray drying the solution to form a dried powder;
- (c) contacting the dried powder with SF<sub>6</sub>; and
- (d) mixing the freeze dried or spray dried powder with an aqueous carrier phase.

36. A method of preparing a dry formulation of an ultrasound contrast agent, wherein upon dissolution in an aqueous carrier liquid, the dry formulation will form a suspension of microbubbles comprising SF<sub>6</sub> and saturated phospholipid, wherein

the amount of the saturated phospholipid in the suspension is less than about 0.01% by weight, the method comprising:

- (a) dissolving at least one saturated phospholipid, a fatty acid, and a hydrophilic stabilizer in an organic solvent to form a solution;
- (b) freeze drying or spray drying the solution to form a dried powder; and
- (c) contacting the dried powder with SF<sub>6</sub>.

37. A method of preparing a dry formulation of an ultrasound contrast agent, wherein upon dissolution in an aqueous carrier liquid, the dry formulation will form a suspension of microbubbles comprising SF<sub>6</sub> and saturated phospholipid, wherein the amount of the saturated phospholipid in the suspension is less than about 0.01% by weight, the method comprising:

- (a) dissolving at least one saturated phospholipid and a hydrophilic stabilizer in an organic solvent to form a solution;
- (b) freeze drying or spray drying the solution to form a dried powder;
- (c) mixing the dried powder with a fatty acid to form a mixture; and
- (d) contacting the mixture with SF<sub>6</sub>.

38. An ultrasound contrast agent comprising an aqueous suspension of gas filled microbubbles comprising a saturated phospholipid, a preserving agent, SF<sub>6</sub>, and a hydrophilic stabilizer, wherein the amount of saturated phospholipid in the suspension is less than about 0.01% by weight, and the preserving agent comprises a fatty acid.



39. The ultrasound contrast agent of claim 38, wherein the preserving agent is present in an amount between 1% and 50% by weight of the amount of the saturated phospholipid.

40. The ultrasound contrast agent of claim 38, wherein the preserving agent is present in an amount between 5% and 25% by weight of the amount of the saturated phospholipid.

41. The ultrasound contrast agent of claim 38, wherein the preserving agent is present in an amount between 10% and 15% by weight of the amount of the saturated phospholipid.

42. The ultrasound contrast agent of claim 38, wherein the preserving agent is a C<sub>12</sub>-C<sub>24</sub> straight chain saturated fatty acid selected from the group consisting of lauric acid, myristic acid, palmitic acid, stearic acid, arachidic acid, behenic acid, lignoceric acid and mixtures thereof.

43. The ultrasound contrast agent of claim 38, wherein the preserving agent comprises palmitic acid in an amount between 10% and 15% by weight of the amount of the saturated phospholipid.

44. The ultrasound contrast agent of claim 38, wherein the saturated phospholipid is selected from the group consisting of dimyristoylphosphatidic acid, dimyristoylphosphatidylglycerol, dimyristoylphosphatidylserine, dipalmitoylphosphatidic acid, dipalmitoylphosphatidylglycerol,

dipalmitoylphosphatidylserine, distearoylphosphatidic acid, distearoylphosphatidylglycerol, distearoylphosphatidylserine and mixtures thereof.

45. The ultrasound contrast agent of claim 38, wherein the saturated phospholipid comprises distearoylphosphatidylcholine (DSPC) and dipalmitoylphosphatidylglycerol (DPPG).

46. The ultrasound contrast agent of any one of claims 38, 43 or 45, wherein the hydrophilic stabilizer comprises PEG 4000.

47. The ultrasound contrast agent of claim 38, wherein the saturated phospholipid comprises distearoylphosphatidylcholine (DSPC) and dipalmitoylphosphatidylglycerol (DPPG), the preserving agent comprises palmitic in an amount between 10% and 15% by weight of the amount of the saturated phospholipid, and the hydrophilic stabilizer comprises PEG 4000.

48. A dry formulation of an ultrasound contrast agent comprising a saturated phospholipid, a preserving agent, and a hydrophilic stabilizer, wherein the preserving agent comprises a fatty acid, and upon dissolution in an aqueous carrier liquid, the dry formulation will form a suspension of microbubbles comprising SF<sub>6</sub> in which the amount of saturated phospholipid in the suspension is less than about 0.01% by weight.

49. The dry formulation of claim 48, wherein the preserving agent is present in an amount between 1% and 50% by weight of the amount of the saturated phospholipid.
50. The dry formulation of claim 48, wherein the preserving agent is present in an amount between 5% and 25% by weight of the amount of the saturated phospholipid.
51. The dry formulation of claim 48, wherein the preserving agent is present in an amount between 10% and 15% by weight of the amount of the saturated saturated phospholipid.
52. The dry formulation of claim 48, wherein the preserving agent is a C<sub>12</sub>-C<sub>24</sub> straight chain saturated fatty acid selected from the group consisting of lauric acid, myristic acid, palmitic acid, stearic acid, arachidic acid, behenic acid, lignoceric acid and mixtures thereof.
53. The dry formulation of claim 48, wherein the preserving agent comprises palmitic acid in an amount between 10% and 15% by weight of the amount of the saturated phospholipid.
54. The dry formulation of claim 48, wherein the saturated phospholipid is selected from the group consisting of dimyristoylphosphatidic acid, dimyristoylphosphatidylglycerol, dimyristoylphosphatidylserine, dipalmitoylphosphatidic acid, dipalmitoylphosphatidylglycerol,

dipalmitoylphosphatidylserine, distearoylphosphatidic acid, distearoylphosphatidylglycerol, distearoylphosphatidylserine and mixtures thereof.

55. The dry formulation of claim 48, wherein the saturated phospholipid comprises distearoylphosphatidylcholine (DSPC) and dipalmitoylphosphatidylglycerol (DPPG).

56. The dry formulation of any one of claims 48, 53 or 55, wherein the hydrophilic stabilizer comprises PEG 4000.

57. The dry formulation of claim 48, wherein the saturated phospholipid comprises distearoylphosphatidylcholine (DSPC) and dipalmitoylphosphatidylglycerol (DPPG), the preserving agent comprises palmitic acid in an amount between 10% and 15% by weight of the amount of the saturated phospholipid, and the hydrophilic stabilizer comprises PEG 4000.

58. A method of using the dry formulation of any one of claims 48 to 55 or 57 for the preparation of an ultrasound contrast agent comprising forming a suspension of gas filled microbubbles from the dry formulation.

59. A method of preparing an ultrasound contrast agent comprising reconstituting the dry formulation of any one of claims 48 to 55 or 57 in an aqueous carrier liquid to form a suspension of gas filled microbubbles.

60. A method of imaging a region of a body comprising:

- (a) reconstituting the dry formulation of any one of claims 48 to 55 or 57 in an aqueous carrier liquid to form a suspension of gas filled microbubbles;
- (b) administering the suspension of gas filled microbubbles to the body; and
- (c) imaging the body.